The eCTD Backbone Files Specification for Study Tagging Files

Revision History

Date	Version	Summary of Changes
2003-08-13	1.0	Original version
2004-03-09	1.1	Clarifications to the original version. Constrains from original version including redundancy of information found in the index.xml file. Added duration category and values. Added "other" as route of administration value. Added new name attribute values for file tag element.

The eCTD Backbone File Specification for Study Tagging Files (STF)

This document provides specifications for creating the electronic common technical document (eCTD) backbone file for the study tagging files for use with the guidance to industry: *Providing Regulatory Submissions in Electronic Format — Human Pharmaceutical Applications and Related Submissions.* This specification is based on the ICH STF DTD. Based on early experience, the flexibility of the ICH STF DTD leads to valid permutations that interfere with the proper functioning of viewing tools. As a result, this specification describes constraints on the ICH STF DTD to reduce the variability of the STF XML file. In addition, this specification includes attribute values not included in the STF style sheet and eliminates some redundant information found in the index.xml file (e.g., title, path).

In order to efficiently process and review applications, information is needed on each document including the document title, subject matter (defined by the headings under which the documents are located in the table of contents), relationship to other documents (e.g., all documents for a specific study report are related to one another), revision information (i.e., new, replace, deleted, append), the location of the document and information on the submission that included the document. The eCTD backbone files (i.e., index.xml and us-regional.xml) include the details on the submission, the subject matter for some documents, the document title, revision information and location of the document. However, the eCTD backbone files do not contain adequate information on the subject matter of many document (e.g., study report documents) and the relationship of the document to other documents. This additional information is provided in the STF.

The STF information not found in the Module 2 to 5 eCTD Backbone File (i.e., index.xml) are essential for study documents provided with electronic submissions to be efficiently archived, processed and reviewed by FDA. A STF should be provided with the submission of any study file. The STF provides for additional heading elements and heading attributes. In the STF, *heading* elements are called *file-tags* and are included in the *doc-content* element. Heading attributes are included in the *document-identifier* element.

I. START AND STOP OF THE STF

The STF is an XML instance controlled by the ICH STF Document Type Definition (DTD). The most recent DTD can be found on the ICH web site (www.ich.org). The DTD should be placed in the *dtd* subfolder of the *util* folder. The stylesheet should be in the *style* subfolder of the in the *util* folder. You should provide a separate STF for each study in a submission. The name for the STF XML file should start with the term "stf-" followed by the alphanumeric code used by the sponsor to unambiguously identify the study (i.e., doc-id described below) and include ".xml" to complete the file name.

For every submission that includes a file for a specific study, you should provide a STF file. You should place the STF for the specific study in the module folder with the

corresponding study files. You should place a *leaf* element in the Module 2 to 5 eCTD Backbone File for each STF. In the corresponding Module 2 to 5 eCTD Backbone File, the STF's *operation* attribute should have a value of "new" for the first STF for a specific study and "append" for any subsequent STF for the same study. Use the study identifier (i.e., doc-id described below) for the title of the leaf. The STF should only include information on the study documents provided with the new submission.

The STF root element is *ectd:study*. The STF header root element contains all the other elements included in the STF. The header root element and the last element of a STF are always the same. They contain information about the following:

1. Version of XML being used
2. Type of characters that are allowed in the file
3. Location of the standards that control the organization of the STF
4. Indication that the file information is ended (end tag)

A sample of the header root element and last line of the STF is provided below:

```
<?xml version="1.0" encoding="UTF-8"?>
<?xml-stylesheet type="text/xsl" href="../util/style/ich-stf-
stylesheet.xsl"?>
<!DOCTYPE ectd:study SYSTEM "../util/dtd/ich-stf.dtd">
<ectd:study xmlns:ectd="http://www.ich.org/ectd" xml:lang="en" dtd-
version="2.0" xmlns:xlink="http://www.w3c.org/1999/xlink">
<!--All the elements will be provided after these elements and before the
last element closing tag named </ectd:study> -->
</ectd:study>
```

II. DOCUMENT-IDENTIFIER ELEMENT

Information describing the study is contained in the *document-identifier* element. There are three elements contained in the *document-identifier* element: *title*, *doc-id*, and *category*.

A. Title Element

The *title* element contains the full study title.

B. Doc-id Element

The *doc-id* is the internal alphanumeric code used by the sponsor to unambiguously identify this study.

C. Category Element

This element is similar to the attributes for the *heading* element in the Module 2 to 5 eCTD Backbone File. This element is only needed for studies that are divided by category that are listed below.

- 4.2.3.1 Single dose toxicity (grouped by species and route of administration)
- 4.2.3.2 Repeat dose toxicity (grouped by species, route of administration, and duration)
- 4.2.4.1 Long term [carcinogenicity] studies (grouped by species)
- 5.3.5.1 Study reports and related information of controlled clinical studies pertinent to the claimed indication (grouped by type of control)

Other studies do not need any category elements. When needed, you should place the *category* elements at the same level as the *title* and *doc-id* elements. They each have one attribute named *name* and *info-type*. The value of the *name* attributes and the corresponding category elements should be selected from the following table. For the value of the *info-type* attribute, use the "ich-e3" if using the ICH recommended value or "fda" if not defined in ICH .

Category Element Attributes and Values	**values for "category" element content choices**
name="species"	
Info-type="ich-e3"	mouse
Info-type="ich-e3"	rat
Info-type="ich-e3"	other-rodent
Info-type="ich-e3"	rabbit
Info-type="ich-e3"	dog
Info-type="ich-e3"	nonhuman-primate
Info-type="ich-e3"	other-nonrodent-mammal
Info-type="ich-e3"	nonmammal
Name="route-of-admin"	
Info-type="ich-e3"	oral
Info-type="ich-e3"	intravenous
Info-type="ich-e3"	intramuscular
Info-type="ich-e3"	intraperitoneal
Info-type="ich-e3"	subcutaneous
Info-type="ich-e3"	inhalation
Info-type="ich-e3"	topical
Info-type="fda"	other
Name="duration"	
Info-type="fda"	short
Info-type="fda"	medium
Info-type="fda"	long
Name="type-of-control"	
Info-type="ich-e3"	placebo
Info-type="ich-e3"	no-treatment-control
Info-type="ich-e3"	dose-response-without-placebo
Info-type="ich-e3"	active-control-without-placebo
Info-type="ich-e3"	external-control

The following is an example of the study elements is provided that indicates a long term carcinogenicity study was conducted using the mouse. (species="mouse"):

<document-identifier>
<title>Long term carcinogenicity study</title>
<doc-id>abc123xyz789</doc-id>
<category name="species"info-type=”ich-e3” >mouse</category>
</category>
</document-identifier>

III. DOCUMENT AND DOC-CONTENT ELEMENTS

The *document* element contains information on the subject matter of a file that is part of the study. The document element includes the *doc-content* element. The *doc-content* element, contains the *property* and *file-tag* elements.

A. Property element

The *property* element should have the *name* and *info-type* attribute. The *property* element value should be the ID value from the *index.xml* file for the file to be tagged with the *file-tag* element. For the value of the *info-type* attribute, use “ich-e3” if using an ICH recommended value or “fda” if the value is not defined in ICH. In the following example, the backbone for sequence number 0005 includes a legacy study report in a file called LegStudy.pdf with index.xml ID of id1002. The *property* element describing this should look like:

<property name=”leaf-id” info-type=”fda” >../../../0005/index.xml#id1002</property>

(note: the “../../../” represents the relative path from the location of the STF file in the submission to return to the index.xml file.

B. File-tag element

The *file-tag* element contains the attributes *name* and *info-type.* The text value of the *file-tag* element's *name* attribute indicates the subject matter of the document. The value of the *file-tag name* attribute should be selected from the values in the table below. For the value of the *info-type* attribute, use “ich-e3” if using an ICH recommended value or “fda” if the value is not defined in ICH . The table below shows the specified *name* attribute values for the *file-tag* element.

name attribute values for the file-tag element (name=” ”)	info-type value	Content of Document
legacy-study-report	ich-e3	Complete study report.
synopsis	ich-e3	Study Report Synopsis (e.g., E3 2)
study-report-body	ich-e3	Study Report Body (e.g., E3 1, 3 to 15)

name attribute values for the file-tag element (name=" ")	info-type value	Content of Document
protocol-or-amendment	ich-e3	Protocol and/amendments (e.g., E3 16.1.1)
sample-case-report-form	ich-e3	Sample CRF (e.g., E3 16.1.2)
iec-erb-consent-form-list	ich-e3	IEC and IRB and Consent Form Listings (e.g., E3 16.1.3)
list-description-investigator-site	ich-e3	Description of Investigators (e.g., E3 16.1.4) and Sites
signatures-investigators	ich-e3	Signatures of principal or coordinating investigator(s) or sponsor's responsible officer (e.g., E3 16.1.5)
list-patients-with-batches	ich-e3	Listing of patients receiving test drug(s) from specified batch (e.g., E3 16.1.6)
randomisations-scheme	ich-e3	Randomisations Scheme (e.g., E3 16.1.7)
audit-certificates-report	ich-e3	Audit Certificates (e.g., E3 16.1.8) or similar documentation
statistical-methods-interim-analysis-plan	ich-e3	Documentation of statistical methods and interim analysis plans (e.g., E3 16.1.9)
inter-laboratory-standardisation-methods-quality-assurance	ich-e3	Documentation of Inter-laboratory Standardization Methods and Quality Assurance (e.g., E3 16.1.10) or similar documentation
publications-based-on-study	ich-e3	Publications Based on the Study (e.g., E3 16.1.11)
publications-referenced-in-report	ich-e3	Publications Referenced in the Study Report (e.g., E3 16.1.12)
discontinued-patients	ich-e3	Discontinued Patients Listing (e.g., E3 16.2.1)
protocol-deviations	ich-e3	Protocol Deviation Listing (e.g., e.g., E3 16.2.2)
patients-excluded-from-efficacy-analysis	ich-e3	Patients Excluded from Efficacy Analysis Listing (e.g., E3 16.2.3)
demographic-data	ich-e3	Demographic Data Listing (e.g., E3 16.2.4)
compliance-and-drug-concentration-data	ich-e3	Compliance and/or Drug Concentration Data Listing (e.g., E3 16.2.5)
individual-efficacy-response-data	ich-e3	Individual Efficacy Response Data Listing (e.g., E3 16.2.6)
adverse-event-listings	ich-e3	File contains Adverse Event Listings (E3 16.2.7)
listing-individual-laboratory-measurements-by-patient	ich-e3	Individual Laboratory Measurements Listed by Patient (e.g., E3 16.2.8)
case-report-forms	ich-e3	CRF for an individual subject (e.g., E3 16.3). You should also provide a "property" element, described below, with its "name" attribute = "site-identifier" and its value the site identification where the study was performed.
data-tabulation-dataset	fda	Data tabulation dataset
data-tabulation-data-definition	fda	Data definitions for data tabulation datasets
data-listing-dataset	fda	Data listing dataset
data-listing-data-definition	fda	Data definitions for data listing datasets

name attribute values for the file-tag element (name=" ")	info-type value	Content of Document
analysis-dataset	fda	Analysis datasets
analysis-program	fda	Program file for analysis dataset
analysis-data-definition	fda	Data definition for analysis datasets
annotated-crf	fda	Annotated CRF for datasets
ecg	fda	Annotated ECG waveform dataset
image	fda	Image files
subject-profiles	fda	Subject profile. You should also provide a "property" element, described below, with its "name" attribute = "site-identifier" and its value the site identification where the study was performed.
safety-report	fda	IND safety report
antibacterial	fda	Antibacterial microbiology report
special-pathogen	fda	Special pathogens (e.g., fungi, parasites, mycobacteria) and immune modulator microbiology report
antiviral	fda	Antiviral microbiology report
iss	fda	Integrated analysis of safety – integrated summary of safety report
ise	fda	Integrated analysis of efficacy – integrated summary of efficacy report
pm-description	fda	Postmarketing periodic adverse event drug experience report description

When you use a *file-tag* element with the *name* attribute value of "subject-profile" or "case-report-forms", you should include a *property* element with the *name* attribute value "site-identifier" and *info-type* value "fda". The content of the *property* element should be text that identifies the site.

IV. EXAMPLE XML

A sponsor is submitting portions of a placebo controlled study titled "Wonderdrug Study S107" performed under their in-house unique identification "S107". In submission sequence number 0005, the sponsor has included a synopsis, the body of the study report and a single case report form from site 111. The corresponding STF is named "STF-S107.XML" and follows:

```
<?xml version="1.0" encoding="UTF-8"?>
<?xml-stylesheet type="text/xsl" href="../util/style/ich-stf-stylesheet.xsl"?>
<!DOCTYPE ectd:study SYSTEM "../util/dtd/ich-stf-1-0a.dtd">
<ectd:study xmlns:ectd="http://www.ich.org/ectd" xml:lang="en" dtd-version="2.0"
xmlns:xlink="http://www.w3c.org/1999/xlink">
    <document-identifier>
        <title>Wonderdrug Study S107</title>
        <doc-id>S107</doc-id>
        <category name="type-of-control" info-type="ich-e3" >placebo</category>
```

```
    </document-identifier>
    <document>
        <doc-content >
            <property name="leaf-id"
                info-type=”fda” >../../../0005/index.xml#id1020</property>
            <file-tag name="synopsis"info-type=”ich-e3”</file-tag>
        </doc-content>
        <doc-content >
            <property name="leaf-id"
                info-type=”fda”>../../../0005/index.xml#id1021a</property>
            <file-tag name="study-report-body" info-type=”ich-e3”</file-tag>
        </doc-content>
        <doc-content>
            <property name-“leaf-id”
                info-type=”fda”>../../../0005/index.xml#id1021b</property>
            <property name=”site-identifier” info-type=”fda”>111</property>
            <file-tag name="case-report-forms" info-type=“ich-e3"</file-tag>
        </doc-content>
    </document>
</ectd:study>
```